

AMENDMENTS TO THE CLAIMS

Please amend claims 2, 10, 12-15, 21, 25, 27, 28, 31, 47, 48, 56, 57, 77, 78, 80, 81, 88, 98 and 101 and please cancel without prejudice or disclaimer claims 3-9, 11, 16-20, 22-24, 26, 29, 30, 32-39, 43, 44, 49-55, 58-76, 87, 89-95, 97 and 100 as follows.

The following listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Original) A process for producing a blood plasma-derived l α lp composition comprising a mixture of inter-alpha inhibitor protein (I α I) and pre-alpha protein (P α I), wherein the I α I and the P α I are present in said mixture in a physiological proportion, the process comprising:

isolating from blood plasma a plasma fraction containing I α I and P α I, wherein the I α I and P α I are present in a physiological proportion; and

purifying the plasma fraction to obtain an l α lp composition with a purity of l α lp ranging from about 85% to about 100% pure.

2. (Currently Amended) The process of claim 1, wherein the isolating ~~is by~~ comprises solid phase extraction, extraction or chromatographing blood plasma.

Claims 3-9. (Cancelled)

10. (Currently Amended) The process of ~~any preceding claim 1~~, wherein the plasma fraction comprises a side fraction obtained from the purification of clotting factor IX or from the purification of a prothrombin complex concentrate.

11. (Cancelled)

12. (Currently Amended) The process of ~~any preceding claim 1~~, wherein the plasma fraction is isolated as a cryosupernatant resulting from cryoprecipitation of blood plasma.

13. (Currently Amended) The process of ~~any preceding claim 1~~, wherein the plasma fraction is cryo-poor plasma.

14. (Currently Amended) The process of ~~any preceding claim 1~~, wherein the plasma fraction is human, primate, bovine, porcine, feline, or canine.

15. (Currently Amended) The process of ~~any preceding claim 1~~, further comprising obtaining blood, obtaining blood plasma, obtaining a side fraction obtained from the purification of clotting factor IX, obtaining a side fraction from the purification of a prothrombin complex concentrate, obtaining a cryosupernatant resulting from cryoprecipitation of blood plasma or obtaining cryo-poor plasma.

Claims 16-20. (Cancelled)

21. (Currently Amended) The process of ~~any preceding claim 1~~, wherein the purifying is by hydroxylapatite chromatography, affinity chromatography or a combination thereof.

Claims 22-24. (Cancelled)

25. (Currently Amended) The process of ~~any preceding claim 1~~, wherein the *IaI* and *PaI* present in the plasma fraction have an apparent molecular weight of between about 60,000 to about 280,000 kDa.

26. (Cancelled)

27. (Currently Amended) The process of ~~any preceding~~ claim 1, further comprising: further purifying the plasma fraction; virus inactivating the plasma fraction and/or the purified l α lp; the addition of stabilizers; comprising pasteurization of the purified l α lp; or anion-exchange chromatography of the purified l α lp.

28. (Currently Amended) The process of claim 27, wherein: the further purifying the plasma fraction is by passing ~~to~~through heparin affinity column and collecting the flow through (unbound) fraction; the virus inactivating is by a solvent/detergent treatment or thermal inactivation; and the anion-exchange chromatography of the purified l α lp is DEAE Sepharose.

Claims 29-30. (Cancelled)

31. (Currently Amended) The process of claim ~~30~~28, wherein the thermal inactivation ~~is~~comprises pasteurization at a temperature of between about 55 to about 65°C or dry heat at 70 to 120°C.

Claims 32-39. (Cancelled)

40. (Original) A composition of l α lp comprising a mixture of inter-alpha inhibitor protein (I α I) and pre-alpha protein (P α I), wherein the I α I and the P α I are present in said mixture in a physiological proportion ranging from about 85% to about 100% pure.

41. (Original) The composition of claim 40, wherein the l α lp comprises between about 60% to about 80% I α I and between about 40% to about 20% P α I.

42. (Original) The composition of claim 40, wherein the physiological proportion is the ratio of I α I to P α I that appears naturally in human plasma.

Claims 43-44. (Cancelled).

45. (Original) The composition of claim 40, further comprising a stabilizing agent.

46. (Original) The composition of claim 45, wherein the stabilizing agent is albumin, polyethylene glycol, alpha,alpha-trehalose, amino acids, salts, glycerol, omega-amino acids, sugar, or combinations thereof.

47. (Currently Amended) A composition of *lalp* comprising a mixture of inter-alpha inhibitor protein (*lal*) and pre-alpha protein (*Pal*), wherein the *lal* and the *Pal* are present in said mixture in a physiological proportion and: have a high trypsin inhibitory specific activity; have a half life of greater than one hour; comprise a light chain of inter-alpha inhibitor protein associated with at least one of three heavy chains H1, H2 and H3; or comprise a light chain of inter-alpha inhibitor protein associated with at least one of three heavy chains H1, H2, H3 and H4.

48. (Currently Amended) The composition of claim 47, wherein the ~~*lalp*~~ comprises between about 60% to about 80% *lal* and between about 40% to about 20% *Pal* the trypsin inhibitory specific activity is between about 1000 to about 2000 IU/mg.

Claims 49-55. (Cancelled)

56. (Currently Amended) The composition of claim [54]~~47~~, wherein the *lalp* composition has a half life of at least 5 hours.

57. (Currently Amended) The composition of claim [54]~~47~~, wherein the *lalp* composition has a half life of at least 10 hours.

Claims 58-76. (Cancelled)

77. (Currently Amended) A composition of *lalp* comprising a mixture of inter-alpha inhibitor protein (*lal*) and pre-alpha protein (*Pal*), wherein the *lal* and the *Pal* are

present in said mixture in a physiological proportion ~~that is made~~, said composition having been prepared by the process according to ~~any of~~ claim[s] 1[-39].

78. (Currently Amended) The composition of ~~any of~~ claim[s] 40[-77], further comprising an additional therapeutic agent.

79. (Original) The composition of claim 78, wherein the additional therapeutic agent is an anticancer agent, an anti-inflammatory agent, an anti-coagulant or an immunomodulator.

80. (Currently Amended) A pharmaceutical composition comprising a therapeutically effective amount of the composition of ~~any of~~ claim[s] 40, 47, 54, 63, 70 or 77 and a pharmaceutically acceptable carrier.

81. (Currently Amended) A method of treating an inflammation related disorder, cancer, or an infectious disease in a subject comprising, administering a therapeutically effective amount of ~~l_αlp produced by the process of any~~ the composition of claim[s] 1-39]40 or 77.

82. (Original) The method of claim 81, wherein the l_αlp is isolated from a subject.

83. (Original) The method of claim 82, wherein the subject is a human, cow, pig, goat, or primate.

84. (Original) The method of claim 81, wherein the l_αlp is administered as a tablet, capsule, or injectables.

85. (Original) The method of claim 81, wherein the l_αlp is at least 85% pure.

86. (Original) The method of claim 81, wherein the l_αlp is between about 85% to about 100% pure.

87. (Cancelled)

88. (Currently Amended) A method of treating a subject for acute inflammatory disease, sepsis, severe shock, septic shock, rheumatoid arthritis, cancer, cancer metastasis, infectious disease, or preterm labor, comprising:

(a) determining the pre-treatment level of one or more of the following levels in a subject:

- (i) the level of $I\alpha I$;
- (ii) the level of $P\alpha I$;
- (iii) the level of $I\alpha Ip$;
- (iv) the level of H3;
- (v) the level of H4;
- (vi) the level of H1;
- (vii) the level of H2; and
- (viii) the level of LC; and

(b) administering a therapeutically effective amount of ~~$I\alpha Ip$~~ the composition of claim 40 or 77 to the subject.

Claims 89-95 (Cancelled)

96. (Original) A method for predicting a response to an $I\alpha Ip$ therapy, comprising:
assaying a sample obtained from a subject to detect the level of one or more of the following:

- (i) $I\alpha I$;
- (ii) $P\alpha I$;
- (iii) $I\alpha Ip$;
- (iv) H3;
- (v) H4;
- (vi) H1;
- (vii) H2; and
- (viii) LC;

wherein the detected levels identifies a subject that may respond favorable to *lalp* therapy.

97. (Cancelled)

98. (Currently Amended) A method of monitoring the progress of a subject being treated with an *lalp* therapy, comprising:

(a) determining the pre-treatment level of one or more of the following levels, in a subject:

- (i) the level of *lal*;
- (ii) the level of *Pal*;
- (iii) the level of *lalp*;
- (iv) the level of H3;
- (v) the level of H4;
- (vi) the level of H1;
- (vii) the level of H2; and
- (viii) the level of LC;

(b) administering a therapeutically effective amount of ~~*lalp*~~the composition of claim 40 or 77 to the subject; and

(c) determining the level of one or more of the levels in the subject after an initial period of treatment with ~~*lalp*~~the composition,

wherein an increase of the level in the subject following treatment with ~~*lalp*~~the composition indicates that the subject is likely to have a favorable clinical response to treatment with *lalp*.

99. (Original) A kit for *lalp* therapy comprising one or more of the following:

- (i) *lal*;
- (ii) *Pal*;
- (iii) *lalp*;
- (iv) H3;
- (v) H4;

- (vi) H1;
 - (vii) H2; and
 - (viii) LC; and
- instructions for therapeutic use.

100. (Cancelled)

101. (Currently Amended) A kit comprising a composition ~~of any of~~ according to
claim[s] ~~40, 47, 54, 63, 70~~ or 77 and instructions for therapeutic use.